PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing, *day/month/year*: 30 NOV 1999

Applicant's or agent's file reference
P16185PC00 KJS/ALJ/SXH

IMPORTANT NOTIFICATION

International application No.	International filing date	Priority date
PCT/AU 98/00648	14 August 1998	14 August 1997

Applicant
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION *et al*

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P16185PC00 KJS/ALJ/SXH	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International application No. PCT/AU 98/00648	International filing date *(day/month/year)* 14 August 1998	Priority Date *(day/month/year)* 14 August 1997
International Patent Classification (IPC) or national classification and IPC Int. Cl.[6] C12N 15/63, 15/67, 15/86; A61K 39/235		
Applicant COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION *et al*		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 42 (21 pages of description, 5 pages of claims, 15 sheets of drawings and a page of abstract) sheet(s).

3. This report contains indications relating to the following items:

I	[X]	Basis of the report
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[X]	Certain observations on the international application

Date of submission of the demand 10 March 1999	Date of completion of the report 26 November 1999
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No. (02) 6285 3929	Authorized Officer J.H. CHAN Telephone No. (02) 6283 2340

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU 98/00648

I. Basis of the report

1. With regard to the elements of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages , as originally filed,
  pages , filed with the demand,
  pages 1-21 filed with the letter of 11 November 1999.
- [X] the claims, pages , as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages 22-26 , filed with the letter of 11 November 1999.
- [X] the drawings, pages , as originally filed,
  pages , filed with the demand,
  figures/sheets 1/15-15/15, filed with the letter of 11 November 1999.
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , filed with the letter of .

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, was on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	YES
	Claims 1-42	NO
Inventive step (IS)	Claims	YES
	Claims 1-42	NO
Industrial applicability (IA)	Claims 1-42	YES
	Claims	NO

2. Citations and explanations (Rule 70.7)

The abbreviations D1-D10 refer to the documents in the order as they appear in the international search report.

Novelty and inventive step:

The closest prior art are found in documents D7 (Reddy et al 1995) and D8 (Reddy et al 1996). Each of these documents discloses a recombinant porcine adenovirus wherein the E3 region of the adenoviral genome is suggested as being an appropriate site for insertion of a heterologous DNA. D7 contemplates PAV-3 as a vector for foreign genes in swine and D8, the PAV 1-3 as expression vectors. Whilst accepting the applicants' submission that there is no disclosure of any porcine adenovirus constructs in the documents, various controlling elements associated with the E3 regions eg the GC box, the CAAT box and the TATA box, have been disclosed therein. (See for example, page 108 of D8 and page 100 of D7). Such disclosures would enable the skilled addressee to construct a recombinant vector for expression of foreign gene based on PAV 1-3 with high expectation of success. Since the applicants have not stated that there were some unexpected practical difficulties associated with the preparation of such constructs, the invention as defined in claims 1-42 would not be novel and deprived of an inventive merit in the light of the disclosures in documents D7 and D8.

Industrial applicability:

The invention as defined in claims 1-42 is deemed to have industrial applicability.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

(a) Claims 1-28, 31-42 are not fully support by the description.
The description discloses the production of a recombinant porcine adenovirus wherein the whole or part of E 3 region of the adenoviral genome is deleted and replaced with a heterologous DNA sequence of interest. Since the "appropriate site" for the integration into the genome has not been defined in these claims, the scope of these claims includes any site for insertion on the porcine adenoviral genome. The applicants' submissions have stated that at the priority date of the current application, that porcine adenoviruses had not been examined in great detail and that little work had been published on the characterisation of the genome. Consequently, claims to the recombinant porcine adenovirus comprising a DNA of interest which has been stably integrated in any appropriate site on the genome, cannot be fully supported by the description.

(b) The description discloses the state of prior art using the specific format; ie "(name of the author and the year of publication of the article)". Such a format requires a list of bibliography to fully describe these articles. However there is no such list in the specification on file. For this reason the description relating to the prior art is not clear.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A recombinant porcine adenovirus capable of expressing DNA of interest, said DNA of interest being stably integrated into an appropriate site of said recombinant porcine adenovirus genome.

2. A recombinant vector including a recombinant porcine adenovirus stably incorporating, and capable of expressing DNA of interest.

3. A recombinant vector as claimed in claim 2 wherein said recombinant porcine adenovirus is capable of expression of at least one heterologous nucleotide sequence.

4. A recombinant vector as claimed in claims 2 or 3 wherein said recombinant porcine adenovirus includes a live porcine adenovirus having virion structural proteins unchanged from those in a native porcine adenovirus from which said recombinant porcine adenovirus is derived.

5. A recombinant vector as claimed in claims 3 or 4 wherein said at least one heterologous nucleotide sequence is capable of expression as an antigenic polypeptide.

6 A recombinant vector as claimed in claims 3 or 4 wherein said at least one heterologous nucleotide sequence is capable of expression as an immuno-potentiating molecule.

7 A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes antigenic determinants of infectious agents causing intestinal diseases in pigs.

8. A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes antigenic determinants of infectious agents causing respiratory diseases in pigs.

9. A recombinant vector as claimed in claim 5 where said heterologous sequence encodes an antigenic determinant of pseudorabies virus (Aujeszky's disease virus).

10. A recombinant vector as claimed in claim 9 where heterologous sequence encodes an antigenic determinant of glycoprotein D of pseudorabies virus.

11. A recombinant vector as claimed in claim 5 where said heretologous sequence encodes an antigenic determinant of porcine respiratory and reproductive syndrome virus (PRRSV).

12. A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes an antigenic determinant of Hog cholera virus.

13. A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes an antigenic determinant of porcine parvovirus.

14. A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes an antigenic determinant of porcine coronavirus.

15. A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes an antigenic determinant of porcine rotavirus.

16. A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes an antigenic determinant of porcine parainfluenza virus.

17. A recombinant vector as claimed in claim 5 wherein said heterologous nucleotide sequence encodes an antigenic determinant of Mycoplasma hyopneumonia.

18. A recombinant vector as claimed in claim 6 wherein said heterologous nucleotide sequence encodes FLT-3 ligand.

19. A recombinant vector as claimed in claim 6 wherein said heterologous nucleotide sequence encodes interleukin 3 (IL-3).

20. A recombinant vector as claimed in claim 6 wherein said heterologous nucleotide sequence encodes porcine interleukin 4 (IL4).

21. A recombinant vector as claimed in claim 6 wherein said heterologous nucleotide sequence encodes gamma interferon (γIFN).

22. A recombinant vector as claimed in claim 6 wherein said heterologous nucleotide sequence encodes porcine granulocyte macrophage colony stimulating factor (GM-CSF).

23. A recombinant vector as claimed in claim 6 wherein said heterologous nucleotide sequence encodes porcine granulocyte colony stimulating factor (G-CSF).

24. A recombinant vector as claimed in claims 3 or 4 wherein said heterologous nucleotide sequence encodes an antigenic polypeptide and an immuno-potentiating molecule.

25. A recombinant vector as claimed in any one of claims 2 to 24 wherein said recombinant porcine adenovirus is selected from the group consisting of serotypes 3 and 4.

26. A recombinant vector as claimed in any one of claims 2 to 25 wherein DNA of interest is stably integrated into the non-essential regions of the porcine adenovirus genome.

27. A recombinant vector as claimed in any one of claims 2 to 26 wherein DNA of interest is stably integrated into the right hand end of the genome.

28. A recombinant vector as claimed in claim 27 wherein DNA of interest is stably integrated into the right hand end of the genome at map units 97 to 99.5.

29. A recombinant vector as claimed in any one of claims 2 to 26 wherein DNA of interest is stably integrated into the E3 region of the genome.

30. A recombinant vector as claimed in claim 29 wherein DNA of interest is stably integrated into the E3 region of the genome at map units 81-84.

31. A method of producing a recombinant porcine adenovirus vector for use as a vaccine including inserting into a non-essential region of an porcine adenovirus genome, at least one heterologous nucleotide sequence in association with an effective promoter sequence.

32. A method as claimed in claim 31 wherein prior to insertion of said heterologous nucleotide sequence, a restriction enzyme site is inserted into said non-essential region of said porcine adenovirus genome.

33. A recombinant vaccine for generating and/or optimising antibodies or cell mediated immunity so as to provide or enhance protection against infection by an infectious organism in pigs, said vaccine including at least one recombinant porcine adenovirus vector stably incorporating, and capable of expression of at least one heterologous nucleotide sequence, and suitable carriers and/or excipients.

34. A recombinant vaccine as claimed in claim 33 wherein the said at least one heterologous nucleotide sequence is capable of expression as an antigenic polypeptide.

35. A recombinant vaccine as claimed in claim 33 wherein said at least one heterologous nucleotide sequence is capable of expression as an immuno-potentiating molecule.

36. A recombinant vaccine as claimed in claim 33 wherein said heterologous nucleotide sequence encodes an antigenic polypeptide and an immuno-potentiating molecule.

37. A recombinant vaccine as claimed in any one of claims 33 to 36 wherein said carriers and/or excipients are selected such that said vaccine is deliverable in the form of an aerosol spray, an enteric coated dosage unit or an inoculum.

38. A method of producing a recombinant vaccine as claimed in any one of claims 33 to 36 including admixing at least one recombinant porcine adenovirus vector stably incorporating, and capable of expression of at least one heterologous nucleotide sequence together with suitable carriers and/or excipients.

39. A method of vaccination of pigs against disease including administering to said pigs a first recombinant porcine adenovirus vector stably incorporating, and capable of expression of at least one heterologous nucleotide sequence encoding an antigenic determinant of said disease against which vaccination is desired.

40. A method as claimed in claim 39 including administering to said pig a second porcine adenovirus vector including at least one heterologous nucleotide sequence which differs from said at least one heterologous nucleotide sequence incorporated in said first recombinant porcine adenovirus vector.

41. A method as claimed in claim 40 wherein said second porcine adenovirus vector comprises a serotype different to that of said first porcine adenovirus vector.

42. A method as claimed in claim 39 wherein said second porcine adenovirus vector incorporates, and is capable of expression of at least one heterologous nucleotide sequence encoding an immuno-potentiating molecule.